Remarks

The Office Action mailed August 10, 2007 has been received and reviewed. Claims 34 and 84 having been amended, claims 1-33, 45-66, 70, and 83 having been previously canceled, without prejudice, the pending claims are claims 34-44, 67-69, 71-82, and 84-102. Reconsideration and withdrawal of the rejections are respectfully requested.

The amendment of claims 34 and 84 is supported throughout the specification.

The Invention

In the first few weeks of life a newborn avian hatchling is relatively incompetent at producing antibodies in response to antigenic stimuli. During this period, a significant amount of resistance to infectious diseases is provided by passive immunity derived from maternally derived antibodies. These maternal antibodies provide passive immunological protection of the developing chick before active antibody production occurs. However, the presence of maternal antibodies can also interfere with the ability of the young bird to actively respond to an immunogen through a mechanism involving antigen elimination which prevents active immunity to that antigen. Thus, maternal antibodies can act to regulate the immune response by inhibiting development of antibody producing cells.

Food producing animals such as poultry are immunized as a group at a set period of time. However, within a given population of animals, there are generally variations in the level of maternal antibody and maturation of the immune system between individual animals. For example, chicks from a commercial hatchery may come from many different breeding farms, each having different types and different levels of passive maternal antibodies. In fact, chicks from the same breeder flock may have highly variable antibody titers to the same disease agent. This non-uniformity of passive immune protection can significantly influence the effectiveness of a vaccination program.

The present invention circumvents the interfering effects of maternal antibodies while providing a stimulus for active immunity at the point a bird is capable of responding to an

immunogen. For instance, the methods of the present invention include injecting a biocompatible implant into an egg. The biocompatible implant includes an immunogen and a biocompatible matrix material, and the egg includes maternal antibody to the immunogen. The implant provides for sustained release of the immunogen until the maternal antibodies in a bird hatching from the egg are reduced so that the bird is capable of mounting an immune response to the immunogen.

Double Patenting Rejection

Claims 34-44 and 67-69 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,682,754. Upon an indication of otherwise allowable subject matter and in the event this rejection is maintained, Applicants will provide an appropriate response.

The 35 U.S.C. §103 Rejection

The Examiner rejected claims 34, 37, 39-43, 67-69, 83-86, 89, 91-95, and 97-102 under 35 U.S.C. §103(a) as being unpatentable over Emery et al. (U.S. Patent No. 5,830,479) in view of Phelps et al. (U.S. Patent No. 5,339,766) in view of Genovese et al. (1998) in light of Sharma et al. (U.S. Patent No. 4,458,630). The traversal of this rejection is respectfully maintained.

The Office Action notes that the claims have been amended to indicate an egg contains maternal antigens to the antibodies (Office Action at page 7, last paragraph). Applicant believes the Examiner intended to state that an egg contains maternal *antibodies* to the *antigens*, and the remarks in this reply are based on that belief.

There are statements in the Office Action suggesting the Examiner believes that the release of immunogen is sustained until maternal antibody in an egg is sufficiently reduced (see, for instance, the Office Action at page 9: "the instant specification gives preferred protocols of when to innoculate the eggs, assuming that the maternal antibodies are 'sufficiently

reduced' in the egg"). Independent claims 34 and 84 have been amended to clarify that the release of immunogen is sustained until maternal antibody in a bird (not an egg) is reduced so that the bird is capable of mounting an immune response to the immunogen. Thus, the reduction of maternal antibody refers to reduction in a bird that hatches from an egg receiving a biocompatible implant.

Emery et al. provides a vaccine composed of a substantially pure siderophore receptor protein that is useful for immunizing an avian or another animal against infection by gram-negative bacteria (see column 2, lines 13-27). Emery et al. further provides fourteen examples that describe the production and purification of siderophore receptor proteins, vaccination of turkey poults, and the ability of the siderophore receptor protein to provide cross-reactivity to varying immunogens. As noted in the background, siderophores had previously not been used as immunogens due to an inability to extract these proteins. Emery et al. do not teach or suggest injecting a biocompatible implant comprising an implant into an egg comprising maternal antibody to the immunogen, wherein the implant provides for sustained release of the immunogen until the maternal antibodies in a bird hatching from the egg are reduced so that the bird is capable of mounting an immune response to the immunogen (independent claim 1, see also independent claims 69 and 84).

Phelps et al., on the other hand, is not directed to the use of a novel immunogen, but rather provides "a method for injecting eggs to minimize the ingress of air and contaminants, and minimize the leakage of albumin from the egg" (column 3, lines 59-61). The method includes use of a sealant at the point of injection to prevent contamination and minimize leakage. While this is a useful method of administering a variety of materials to an egg, and is in fact incorporated by reference in Applicants' specification, this reference does not teach or suggest providing sustained release of the immunogen until the maternal antibodies in a bird hatching from the egg are reduced so that the bird is capable of mounting an immune response to the immunogen (independent claim 1, see also independent claims 69 and 84).

Genovese et al. present experiments that evaluate the ability of lymphokines to protect day-old turkeys against Salmonella enteritidis liver invasion, induce peripheral blood heterophilia, and functionally activate heterophiles when delivered by subcutaneous, oral, or intranasal routes when compared to intraperitoneal injection (see headnote, page 1 of the Genovese et al. document included with the Office Action dated March 24, 2006). The lymphokines delivered to the turkeys act "as an immunopotentiator during the first 7 days of life in poultry when . . . the immune response of these young birds is incompetent" (Genovese et al., page 5 of the Genovese et al. document included with the Office Action). Genovese et al. do not teach or suggest injecting a biocompatible implant comprising an implant into an egg comprising maternal antibody to the immunogen, wherein the implant provides for sustained release of the immunogen until the maternal antibodies in a bird hatching from the egg are reduced so that the bird is capable of mounting an immune response to the immunogen (independent claim 1, see also independent claims 69 and 84).

Genovese et al. was first cited by the Examiner as evidence that the ordinary artisan would have recognized that the most crucial time of vaccination delivery to a young bird is within the first few days of life. Genovese et al. state vaccines can be used on newly hatched chicks and poults, but "maternal antibodies may cause interference with the vaccine and the desired immune response" (Genovese et al., page 5 of the Genovese et al. document included with the Office Action). Genovese et al. also state that "[o]ne to 7-day-old chicks and poults have been shown to be immunologically incompetent" (Genovese et al. at page 2 of the Genovese et al. document included with the Office Action), and admits that the lymphokines act "during the first 7 days of life in poultry when . . . the immune response of these young birds is incompetent" (Genovese et al., page 5 of the Genovese et al. document included with the Office Action). "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention" (M.P.E.P §2141.02(VI)). Genovese et al. present several statements that vaccinating newly hatched chicks and poults may not result in an immune response. Thus, Genovese et al. cannot be used to support the proposition that

delivery of vaccine to a young bird within the first few days of life is recognized to be a crucial time for vaccination.

Furthermore, Genovese et al. do not administer anything to eggs, and the independent claims recite injecting a biocompatible implant into an egg. Genovese et al. inject the day old chicks, but not with an immunogen. Instead, the day old chicks are treated with lymphokines, which potentiate the innate immunity of poultry (Genovese et al., second paragraph of Introduction).

Sharma et al. teach the use of embryonal vaccination during the final quarter of incubation. Sharma et al. do not teach or suggest injecting a biocompatible implant into an egg, or providing sustained release of the immunogen until the maternal antibodies in a bird hatching from the egg are reduced so that the bird is capable of mounting an immune response to the immunogen (independent claim 1, see also independent claims 69 and 84). In fact, by stating that an embryo becomes immunologically competent in the final quarter of the incubation period (Sharma et al., col. 2, lines 58-64), Sharma et al. teach away from the need to use a biocompatible implant to result in sustained release of the immunogen until the maternal antibodies in a bird hatching from the egg are reduced so that the bird is capable of mounting an immune response to the immunogen.

Sharma et al. was first cited by the Examiner as evidence that a bird's immune response is elicited even in the embryonic stage when vaccinated in-ovo. As argued in the response dated May 15, 2007, the eggs used by Sharma et al. did not include maternal antibody to the antigen administered in the vaccine.

The Examiner notes that Emery et al. teach that siderophore receptor proteins could be used to challenge the immune systems of poultry and eggs, but then asserts that the skilled person would recognize that the siderophore receptor protein could have been used in poultry and subsequently in the poultry's fertilized eggs (Office Action, page 8, second paragraph). The applicant disagrees: the skilled person would recognize that using a siderophore receptor protein in the poultry's fertilized eggs that contained maternal antibody to the

siderophore receptor protein would probably not result in an immune response in the egg or in the bird hatching from the egg due to the presence of maternal antibodies. For at least this reason, the skilled person would not be motivated to combine the methods of Phelps et al. with Emery et al. as argued by the Examiner at page 8 of the Office Action.

Likewise, at page 9 of the Office Action the Examiner states that "[r]egardless of the fact that the egg would or would not contain maternal antibodies to the antigen, the ordinary artisan would have been motivated to further inoculate the eggs produced by this chicken which had been inoculated *in-ovo* because there would be a reasonable expectation that the inoculation would have afforded the unhatched bird some immunity to the antigen." If the eggs contained maternal antibodies to the antigen, the ordinary artisan would expect the presence of the maternal antibodies to interfere with the ability of the bird to mount an immune response. For at least this reason, the skilled person would not be motivated to inoculate eggs with an antigen that would be bound by maternal antibodies in the recipient eggs.

To establish a *prima facie* case of obviousness, there must also be a reasonable expectation of success. A reasonable expectation of success is highly correlated to the predictability of the field of endeavor. Applicants respectfully suggest that immunization can be a highly unpredictable art, and that this unpredictability is further increased by the complex interaction between maternal antibodies and the newborn birds immune systems. Applicants, in the Examples (p. 27 to 35 of the specification) have demonstrated that in ovo immunization can be successfully carried out and that immunization in hatched birds can successfully occur due to sustained release of immunogen. Applicants respectfully suggest that a reasonable expectation of success did not exist prior to Applicant's disclosure, and is not provided by the combination of Emery et. al with Phelps et al.

The Examiner's assertions regarding the reasonable expectation of success include asserting that the skilled person "would have had a reasonable expectation that inoculation of the egg with a siderophore receptor protein would have had a reasonable expectation of success, even though maternal antibodies toward the siderophore receptor protein were present in the

egg" (Office Action, page 8, second paragraph), and "there would be a reasonable expectation that the inoculation would have afforded the unhatched bird some immunity to the antigen" (Office Action, page 9). Genovese et al. state that maternal antibodies may cause interference with the vaccine and the desired immune response, and none of the eggs used by Emery et al. or Sharma et al. included maternal antibodies to the administered antigen. The eggs used in the claimed methods include maternal antibody to the injected immunogen. The Examiner cannot assert that the skilled person had a reasonable expectation of success. For at least these reasons, the Office has failed to establish some predictability in any attempt to combine the cited documents to result in the present invention.

The recent Supreme Court decision KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) was cited by the Examiner to support the proposition that the elements of the claims were known, and were rendered obvious in view of known methods regarding poultry inoculation. The invention in KSR was in the mechanical arts, which is often characterized by the Office as a predictable art. In contrast, the present invention can be considered to be in the biotechnological arts, which is often characterized by the Office as an unpredictable art. The claimed invention is not a predictable variation of the techniques presented in the cited documents. For instance, as discussed hereinbefore, immunization can be a highly unpredictable art.

For at least these reasons, reconsideration and withdrawal of the present rejection is respectfully requested.

The Examiner rejected claims 34-44, 67-69, 71-82, and 84-102 under 35 U.S.C. §103(a) as being unpatentable over Emery et al. (U.S. Patent No. 5,830,479) in view of Phelps et al. (U.S. Patent No. 5,339,766) and further in view of Evans et al. (U.S. Patent No. 6,500,438 B2) in view of Genovese et al. (1998) in light of Sharma et al. (U.S. Patent No. 4,458,630). The traversal of this rejection is respectfully maintained.

The Examiner is requested to note that as discussed hereinbefore, the independent claims are not obvious in view Emery et al., Phelps et al., Genovese et al., and Sharma et al., and

Evens et al. does not supplement any of the deficiencies of Emery et al., Phelps et al., Genovese et al., and Sharma et al. For at least these reasons, reconsideration and withdrawal of the present rejection is respectfully requested.

Summary

It is respectfully submitted that the pending examined claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
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The undersigned hereby certifies that the paper(s), as described hereinabove, are being transmitted via the U.S. Patent and Trademark Office electronic filing system in accordance with37 CFR §1.6(a)(4) to the Patent and Trademark Office addressed to Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 11th day of February, 2008.

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